Australian Government
Department of Health and Ageing
Therapeutic Goods Administration

Manufacturing standards for plasma for fractionation

Australian regulatory requirements

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Australian Government
Department of Health and Ageing
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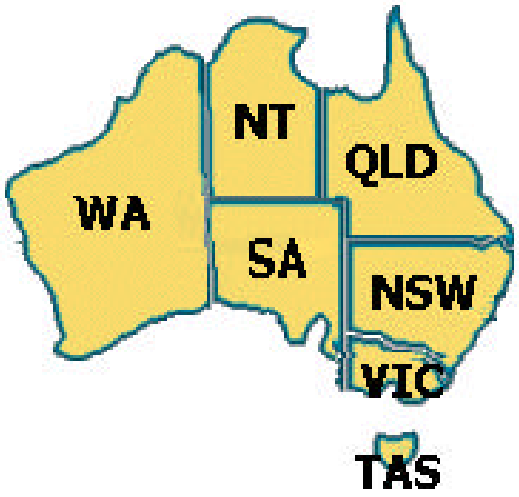
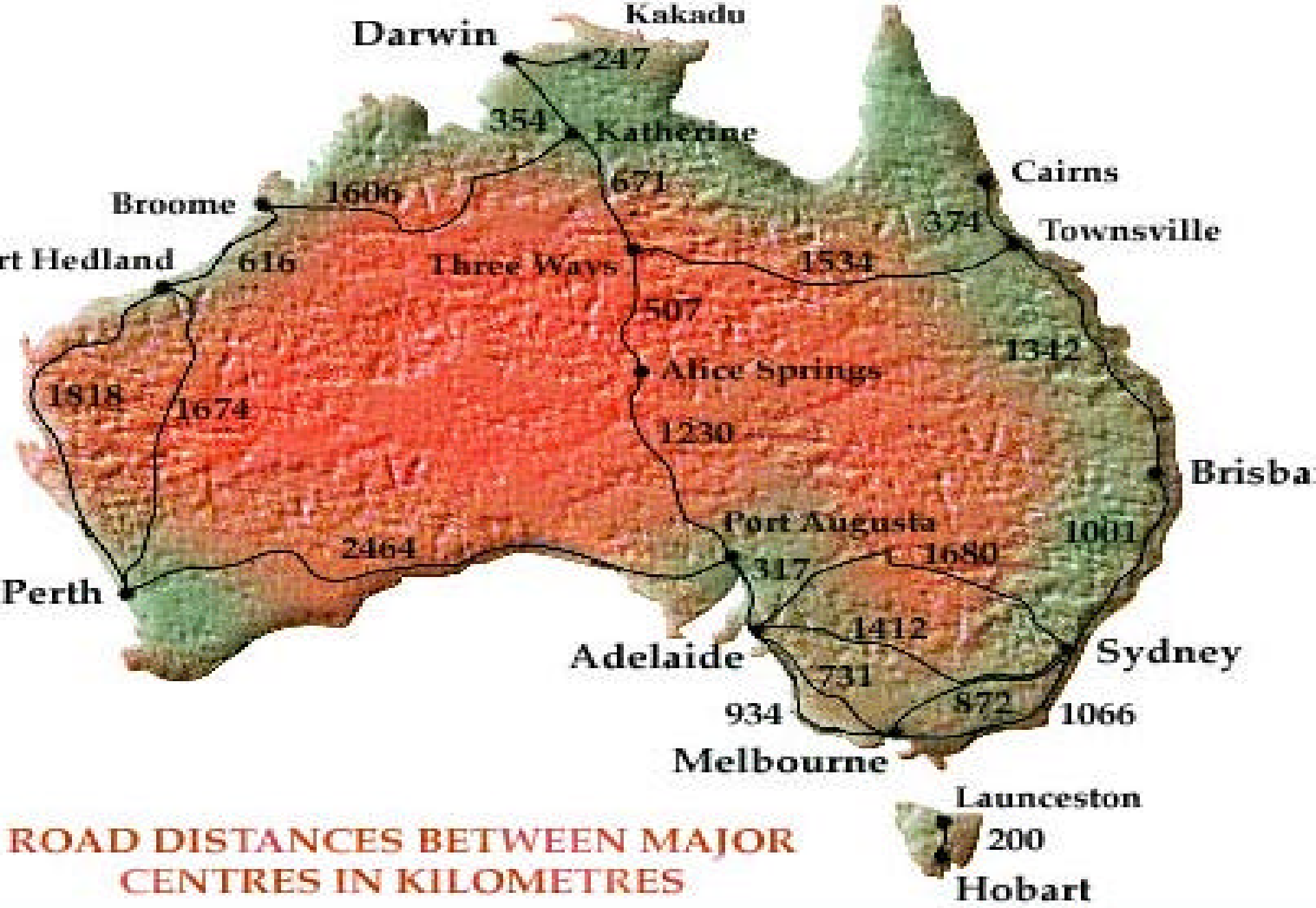
Australia - On top of the world

Australia



- Population 19.4 million
- Federation of States and Territories
- Social market economy
- Govt a primary deliverer of health care
- States actually responsible for services - hospitals etc
- ARCBS - blood agency - funded by all govts



ROAD DISTANCES BETWEEN MAJOR CENTRES IN KILOMETRES

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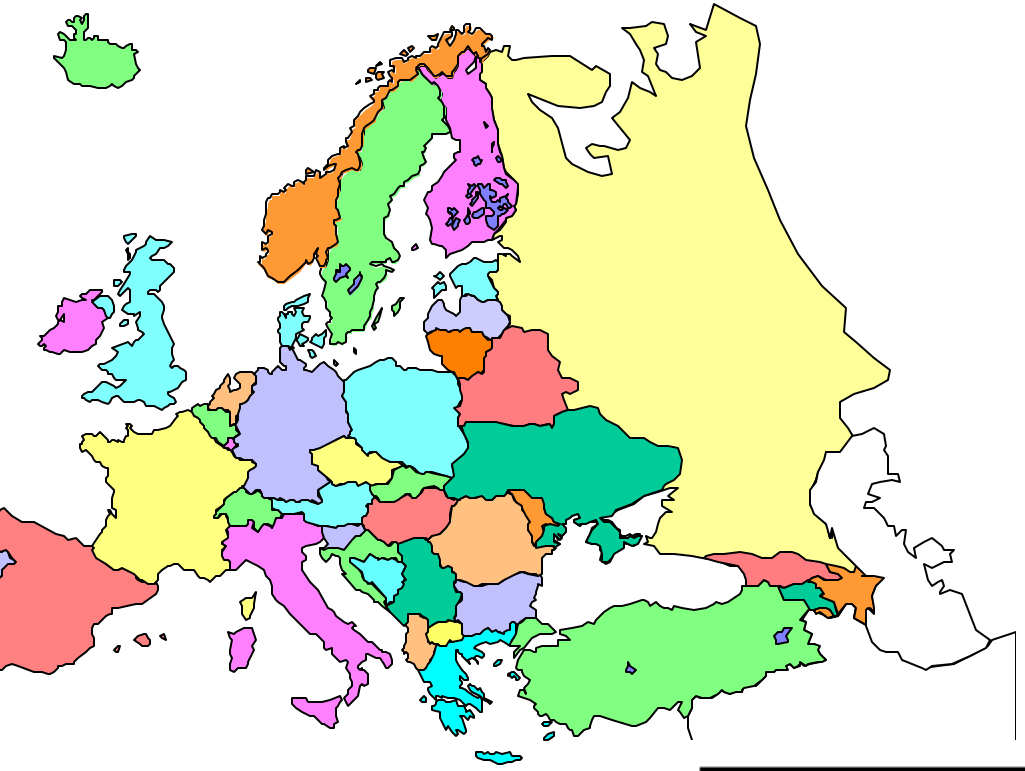
Available standard



2001: 0853

HUMAN PLASMA FOR FRACTIONATION

Plasma humanum ad separationem

When obtained by plasmapheresis, plasma intended for the recovery of proteins that are labile in plasma is frozen by cooling rapidly at – 30 °C or below as soon as possible and at the latest within 24 h of collection.

When obtained from whole blood, plasma intended for the recovery of proteins that are labile in plasma is separated from cellular elements and is frozen by cooling rapidly at – 30 °C or below as soon as possible and at the latest withi 24 h of collection.

When obtained from whole blood, plasma intended solely for the recovery of proteins that are not labile in plasma is separated from cellular elements and frozen at – 20 °C or below as soon as possible and at the latest within 72 h of collection.

…….Store frozen plasma at or below – 20 °C; the plasma may still be used fo fractionation if a temperature of – 20 °C is exceeded on at most one occasion for not more than 72 h and if the plasma is at all times maintained at a temperature of – 5 °C or lower.

Plasma Master File Guideline 2004

2.2.4 Conditions of storage and transport of plasma.

See Annex IV and V.

Describe the conditions for freezing and storage of plasma for every establishme responsible for collecting blood/plasma including the following:

- Sites/organisations which are involved in the storage and indicate whether they hav been inspected by a Competent Authority.
- Compliance with Ph. Eur. with respect to freezing and storage.
- Conditions of storage (temperature and maximum time).

Describe the conditions of transport of plasma including the following:

- Transport flows from centres of collection to interim storage sites, if relevant, ar further to fractionation sites.
- Organisations which are involved in the transport (own and contractors) and indica whether they have been inspected by a Competent Authority.
- Conditions of transport (maximum time and temperature).
- Confirm compliance with requirements in the Ph. Eur. Monograph for Human Plasm

[9] for Fractionation and if applicable, with any Ph. Eur. requirements for particul products.

CONTENT OF THE PMF

Plasma Origin

- *blood/plasma collection establishments [Epidemiology data for viral markers/agents contract between establishment(s) and plasma fractionator/manufacturer(s)]*
- *selection/exclusion criteria of donors (questionnaire)*
- *selection/exclusion criteria(screening tests for infection markers) of donation and pools*
- *plasma tracing (intermediate plasma fractions, variant Creutzfeld-Jakob disease)*

Plasma Quality and Safety

- *blood bags*
- *storage and transportation*
- *pooling (defined pools)*
- *contract arrangements with manufacturer*
- *conformity with EP Monograph / includes those adopted here*

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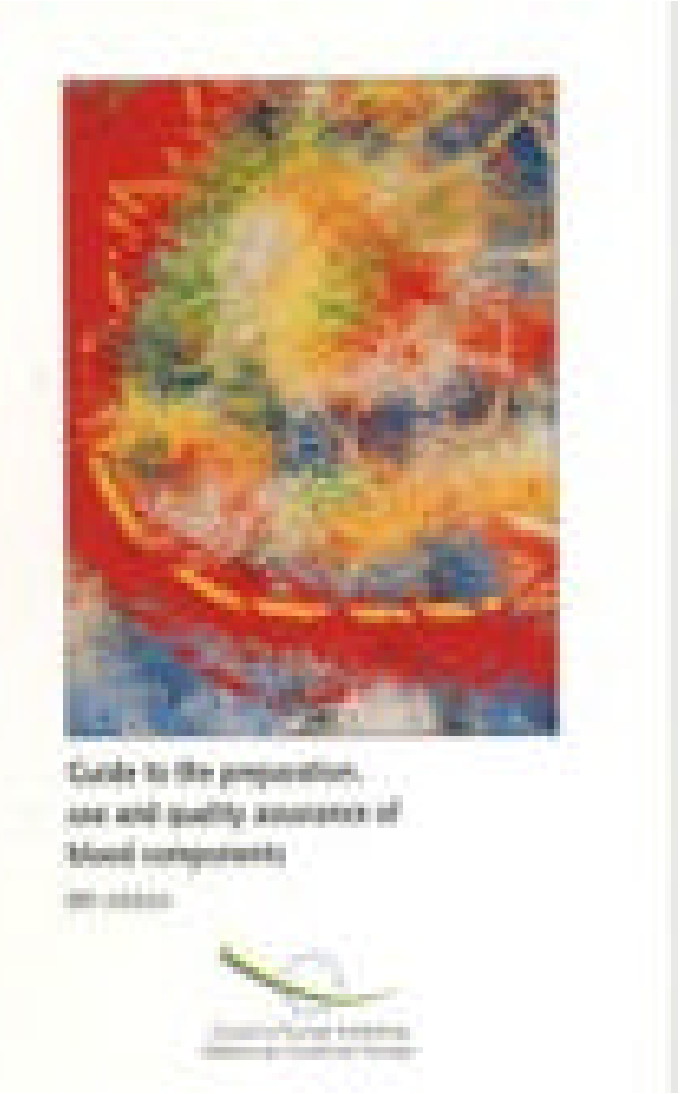
Council of Europe Guide for Blood Components



- Includes chapters on FFP, cryo-poor plasma
- FFP standards sometimes at variance with EP monograph
- NOT APPLICABLE for fractionation - refers to EP monograph

European plasma standards
Freezing

Council of Europe

(for transfusion)

blood storage

- preferably < 6 hours, ≤ 18 hours
- if held ≥ 20°C≤24°C, ≤ 24 hours

plasma freezing - ≤ 1 hour, to -30°C

these requirements hold for both "recovered" and "source" plasma

European Pharmacopeia

(for fractionation)

- blood storage - for labile protein manufacture, ≤ 24 hours, for non-labile protein manufacture ≤ 72 hours
- plasma freezing - for labile protein manufacture to -30°C within 24 hours of collection for non-labile protein manufacture -20°C
- these requirements hold for both "recovered" and "source" plasma

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European plasma standards
Storage

Council of Europe

(for transfusion)

24 months ≤ -25°C

3 months -18°C to - 25°C

European Pharmacopeia

(for fractionation)

Store frozen plasma at or below – 20 °C; the plasma may still be used fo fractionation if a temperature of – 2 °C is exceeded on at most one occasion for not more than 72 h an if the plasma is at all times maintained at a temperature of – 5 or lower

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European plasma standards
FVIII levels

Council of Europe
(for transfusion)

Requirement for ≥ 70% of the "*average normal value*" controlled through measurement of FVIIIc every two months on a pool of six units of mixed blood groups during the first and last months of storage

European Pharmacopeia
(for fractionation)

On a pool of not fewer than t units, measurement of fact VIII, using the EP referen method and a reference plasm calibrated against t International Standard for blo coagulation factor VIII plasma. The activity is not le than 0.7 I.U. per millilitre.

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Australian plasma productio
July 2003-June 2004

Donations of whole blood	907904
Units of recovered plasma	904464
<24 hours post-donation	
→Units of clinical FFP	197554
→Units of plasma for fractionation	706910
Donations of apheresis plasma	150390
→Units of plasma for fractionation	140842

Approx 267 tonnes of plasma for fractionation

Approx 176 tonnes manufactured to FVIII (66%)

Conclusions

Australia aligns to European requirements for both *clinical transfusion plasma* and *plasma for fractionation*

Although the standards for these products are occasionally discordant, in practical terms this has not proved to be insoluble

Despite considerable logistical challenges, the majority of plasma from whole blood donations is recovered within 24 hours of donation